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The Melbourne Consensus Statement on the early detection of prostate cancer

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Introduction

Recent guideline statements and recommendations have led to further confusion and controversy about the use of PSA testing for the early detection of prostate cancer. Despite high-level evidence for the use of PSA testing as a screening tool, and also for its role as a predictor of future risk, the USA Preventive Services Taskforce (USPSTF) has called for PSA testing to be abandoned completely [1], and many men are therefore not given the opportunity for shared decision-making. Other groups, e.g. the AUA [2], National Comprehensive Cancer Network (NCCN) [3], and European Association of Urology (EAU) [4], support a role for PSA screening but with conflicting recommendations. Most guideline statements have endorsed the role of shared decision-making for men considering PSA testing.

To address these conflicting and confusing recommendations, a group of leading prostate cancer experts from around the world came together at the 2013 Prostate Cancer World Congress in Melbourne, Australia, and generated a set of consensus statements about the use of PSA testing and the early detection of prostate cancer. The signatories to the Melbourne Statement include representatives from urology, radiation oncology, medical oncology, general practice, psycho-oncology and nursing. The goal of these statements is to bring clarity to the confusion that exists with existing guidelines and to present reasonable and rational guidance for the early detection of prostate cancer today. These statements are based on an appraisal of existing guideline statements and an overview of published data about the early detection of prostate cancer.

Consensus Statement 1: For Men Aged 50–69 Years, Level 1 Evidence Shows that PSA Testing Reduces the Incidence of Metastatic Prostate Cancer and Prostate Cancer-Specific Mortality Rates

In the European Randomized Study of Screening for Prostate Cancer (ERSPC), still with early follow-up, screening reduced metastatic disease and prostate cancer-specific mortality by up to 30% and 21% respectively in the intent-to-treat analysis, with a greater reduction after adjustment for noncompliance and contamination [5,6]. Statistical modelling studies of ERSPC data have reported that with steady-state application of the ERSPC protocol, that the prostate cancer-specific mortality benefit would reach 67% reduction at the beginning of 12
years of follow-up. In addition, the Göteborg randomised population-based randomised trial showed a reduction in metastatic disease and prostate cancer mortality with screening starting at age 50 years, and the greatest reduction was seen in the youngest age group [7]. The extent of over-diagnosis and over-treatment decreases considerably with longer follow-up, such that the numbers needed to screen (293) and numbers needed to treat (12) to avert one prostate cancer death, compare very favourably with screening for breast cancer. While routine population-based screening is not recommended, healthy, well-informed men in this age group should be fully counselled about the positive and negative aspects of PSA testing to reduce their risk of metastases and death. This should be part of a shared decision-making process.

Consensus Statement 2: Prostate Cancer Diagnosis Must be Uncoupled from Prostate Cancer Intervention

Although screening is essential to diagnose high-risk cases within the window of curability, it is clear that many men with low-risk prostate cancer do not need immediate aggressive treatment. Active surveillance protocols have been developed and have been shown to be a reasonable and safe option for many men with low-volume, low-risk prostate cancer [8–10]. While it is accepted that active surveillance does not address the issue of over-diagnosis, it does provide a vehicle to avoid excessive intervention. Active surveillance strategies need standardisation and validation to ensure that this is a safe strategy and to reassure patients and clinicians.

Consensus Statement 3: PSA Testing Should Not Be Considered on Its Own, But Rather as Part of a Multivariable Approach to Early Prostate Cancer Detection

PSA is a weak predictor of current risk and additional variables, e.g. age, ethnicity, family history, medical history, DRE findings, prostate volume, risk prediction models [11–13] and new tools, such as the Prostate Health Index (phi) test and prostate cancer antigen 3 (PCA3) test, can help to better stratify men, potentially reducing over-diagnosis and over-treatment of indolent prostate cancer. Further developments in the area of biomarkers, as well as improvements in imaging will continue to improve risk stratification, with potential for reduction in over-diagnosis and over-treatment of lower risk disease.

Consensus Statement 4: Baseline PSA Testing for Men in Their 40s is Useful for Predicting the Future Risk of Prostate Cancer and Its Aggressive Forms

Although these men were not included in the two large randomised trials, there is strong evidence that men may benefit from the use of PSA testing as a baseline to aid risk stratification for their likely future risk for developing prostate cancer [14], including clinically significant prostate cancer. Studies have shown the value of PSA testing in this cohort for predicting the increased likelihood of developing prostate cancer 25 years later for men whose baseline PSA level is in the highest centiles above the median [15,16]. For example, those men with a PSA level above the median are at considerably higher risk and need closer surveillance. The median PSA level for men aged 40–49 years ranges from 0.5 to 0.7 ng/mL, with the 75th percentile ranging from 0.7 to 0.9 ng/mL [3,17]. The higher above the median, the greater the risk of later developing life-threatening disease. We recommend that a baseline PSA measurement in the 40s has value for risk stratification and this option should be discussed with men in this age group as part of a shared decision-making process.

Consensus Statement 5: Older Men in Good Health Denied PSA Testing Based on Their Age

Men should be assessed on an individual basis rather than applying an arbitrary chronological age beyond which testing should not occur. As life expectancy improves in many countries around the world (men aged 70 years in Australia have a 15-year life expectancy), a small proportion of older men may benefit from an early diagnosis of more aggressive forms of localised prostate cancer, just as it is clear that men with many competing co-morbidities and less aggressive forms of prostate cancer are unlikely to benefit irrespective of age. Likewise, a man in his 70s who has had a stable PSA level at or below the median for a number of years previously, is at low risk of developing a life-threatening prostate cancer and the screening protocol can be appropriately modified.

Discussion

An important goal when considering early detection of prostate cancer, is to maintain the gains that have been made in prostate cancer-specific survival over the past 20 years since the introduction of widespread PSA testing, while minimising the harms associated with over-diagnosis and over-treatment. This is already happening in Australia, where >40% of patients with low-risk prostate cancer are managed with surveillance or watchful waiting [18], and in Sweden where 59% of very-low-risk patients are on active surveillance. This is also reflected in current guidelines from the EAU, NCCN and other expert bodies. Abandonment of PSA testing as recommended by the USPSTF, would lead to a large increase in men presenting with advanced prostate cancer [19], and a reversal of the gains made in prostate cancer mortality over the past two decades.

However, any discussion about surveillance is predicated on having a diagnosis of early prostate cancer in the first instance. As Dr Joseph Smith editorialised in the Journal of Urology.
after the publication of the ERSPC and the Prostate, Lung, Colorectal, and Ovarian cancer screening (PLCO) trials, ‘treatment or non-treatment decisions can be made once a cancer is found, but not knowing about it in the first place surely burns bridges’ [20,21]. A key strategy therefore is to continue to offer well-informed men the opportunity to be diagnosed early, while minimising harms by avoiding intervention in those men at low risk of disease progression. The Melbourne Consensus Statement (Figure 1) provides some practical guidance to help clinicians and patients achieve these goals as part of a shared decision-making process.

Conflicts of Interest
None disclosed.

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Abbreviations: EAU, European Association of Urology; ERSPC, European Randomized Study of Screening for Prostate Cancer; NCCN, National Comprehensive Cancer Network; USPSTF, USA Preventive Services Taskforce.